

RECEIVED  
CENTRAL FAX CENTER

OCT 19 2006

Serial No. 10/762,895  
Art Unit: 1655**REMARKS**

Applicants respectfully request that the amendments be entered in the specification.

The amendments to the specification refer to the related applications.

In addition, the Abstract has been amended as suggested by the Examiner. Applicants respectfully submit that no new matter has been entered by way of amendment to the specification.

The claims have been amended to delete the term polyol from claim 14 and to indicate that a mixture comprising the organism, substrate and fermentation medium are fermented at a pH up to 7. Commas have been entered in the remaining claims where appropriate. Claim 26 has been canceled since the limitations of claim 26 have been entered in claim 14. Applicants respectfully submit that the amendments to the claims overcome all of the Examiner's rejections under 35 USC 112 and 35 USC 102 and 103. Favorable consideration of the claims in their amended form is respectfully requested.

The application is directed to a process for the production of polycarboxylic acids and hydroxycarboxylic acids by utilizing a certain synthetic fermentation medium. A critical component of the synthetic fermentation medium is a source of biotin, substantially free of particulate matter and bacteria. Applicants have unexpectedly discovered that if a relatively pure source of biotin is utilized, the odor and separation difficulties for recovering the product of the process is substantially reduced. Applicants respectfully submit that none of the prior art references cited by the Examiner utilizes a source of biotin, substantially free of particulate matter and bacteria.

**Serial No. 10/762,895**

**Art Unit: 1655**

Claims 14, 17-26 and 28 stand rejected under 35 USC 102(b) as anticipated by or, in the alternative, under 35 USC 103(a) as obvious over Shirai et al. (US 5,618,708). Applicants respectfully submit that Shirai et al. is not pertinent to the present invention in view of the amendments entered in the claims.

Shirai et al. is directed to the production of inositol which is a polyol vitamin-like compound. The process comprises utilizing a *Candida boidinii* mutant strain of yeast to form the polyol.

The claims have been amended to delete the production of the polyol in view of the teachings of Shirai et al.

Shirai et al. is deficient in neither teaching nor suggestion that the carboxylic acids can be prepared by the process and in addition does not require the use of a source of biotin, substantially free of particulate matter and bacteria. At column 6, beginning at line 14, Shirai et al. teaches:

"As an organic trace component, biotin or other vitamins needed by the microorganism, alone or in combination can be contained in a fermentation medium. The concentration of the organic trace component is preferably 0.000001% to 0.1% according to the nature of the organic trace component. If necessary a material abundantly containing vitamins, amino acids, and other growth factors, for examples, corn steep liquor, peptones, yeast extract etc. can be contained in a medium. The concentration of such a material is preferably 0.01 to 5% according to the nature of the material."

Applicants respectfully submit that this statement would clearly indicate that a source of biotin, essentially free of particulate matter and bacteria is not required in the process. Applicants submit that one skilled in the art would understand that materials such as corn steep liquor, peptones, yeast extract and the like would contain biotin but would not

**Serial No. 10/762,895**

**Art Unit: 1655**

meet the requirements that a source of biotin be substantially free of particulate matter and bacteria. The use of biotin which is substantially particulate and bacteria free provides a fermentation medium which does not cause a significant odor problem during the fermentation and in addition provides a medium from which the polycarboxylic acid can be easily recovered.

In addition, Shirai et al. is deficient in neither teaching or suggesting the formation of a polycarboxylic acid or a hydroxycarboxylic acid. In addition, Applicants submit that Shirai et al. discloses that the polyol is recovered in relatively small amounts from the process (in the range of 1 to 3 grams per liter). Applicants respectfully submit that Shirai et al. would neither teach nor suggest the present invention and a rejection under 35 USC 102(b) or 35 USC 103(a) is untenable and Applicants request that the rejection be reconsidered and withdrawn.

Claims 14-22 and 24-26 stand rejected under 35 USC 102(b) as anticipated by or, in the alternative, under 35 USC 103(a) as obvious over Mobley et al. (US 6,066,480) with evidence provided by Takahashi et al. (1965, Applied Microbiology, Volume 13, pages 1-4). Applicants respectfully submit that Mobley et al. alone or in view of Takahashi et al. neither teaches nor suggests the present invention. Mobley et al. discloses a method for producing  $\alpha,\omega$ -alkanedicarboxylic acids by bioconversion process. However, the process disclosed by Mobley et al. neither teaches nor suggests the present invention.

A critical feature of the present invention is use of a biotin which is substantially particulate and bacteria free. The use of the biotin which is substantially particulate and

**Serial No. 10/762,895**

**Art Unit: 1655**

bacteria free provides a process which produces less odor and from which the product can be readily recovered.

In contrast to the present invention, Mobley et al. utilizes a fermentation medium containing substantial amounts of corn steep liquor. This must obviously be the source of vitamins and biotin used in the process. In addition, Mobley et al. differs from the process of the present in that the mixture of the organism, substrate and fermentation medium is not fermented at a pH in the range up to 7. As shown in all of the examples, when the substrate is introduced into the fermentation medium, the pH is in a range of 7.0 to about 8 and preferably 7.8 (column 8, lines 27 and 28).

Applicants respectfully submit that Mobley et al. would neither teach nor suggest carrying out the conversion at a pH up to 7 and in addition utilizing a source of biotin which is substantially free of particulate matter and bacteria. Applicants respectfully submit that there is neither teaching nor suggestion that there would be any advantage to carrying out the process of the present invention in the pH range claimed and utilizing a source of biotin as presently claimed. Applicants therefore respectfully submit that Mobley et al. neither teaches nor suggests the present invention and a rejection under 35 USC 102(b) or 35 USC 103(a) is untenable and should be reconsidered and withdrawn.

Takahashi et al. does not cure the deficiencies in Mobley et al. Takahashi et al. teaches that biotin has very little effect on accumulation of L-glutamic acid (see abstract) and in addition the source of vitamins as shown in the abstract is corn steep liquor. As shown in Table 1, corn steep liquor has only a small effect on the production of L-glutamic

**Serial No. 10/762,895**

**Art Unit: 1655**

acid in the process. Takahashi et al. found that thiamine is the critical feature of the process and has a significant affect on the production of L-glutamic acid. The critical vitamins are vitamins A and B and thiamine. As shown in Table 3 of Takahashi et al., a number of vitamins were tested and only riboflavine and thiamine had a significant effect on the production of the L-glutamic acid.

The effects disclosed in Takahashi et al. may be due to the particular strain of yeast utilized to carry out the test. However, Applicants respectfully submit that Takahashi et al. provides a conclusion which is far different from the critical feature of the fermentation medium containing biotin. Applicants therefore respectfully submit that Takahashi et al. does not cure the deficiencies in Mobley et al. Applicants request that the rejection be reconsidered and withdrawn.

Claims 14-28 stand rejected under 35 USC 103(a) as obvious over the combination of Shirai et al. in view of Mobley et al. with evidence provided by Takahashi et al. Applicants respectfully submit that Shirai et al., Mobley et al. and Takahashi et al. whether considered alone or in combination neither teach nor suggest the present invention.

The claims have been amended to delete the production of a polyol. Applicants respectfully submit that this eliminates Shirai et al. which is directed to production of inositol which is a six hydroxy group vitamin-like material. In addition, Shirai et al. discloses use of materials such as yeast extract, peptones and the like to provide the biotin-like materials required in the process. Applicants submit that there is neither teaching nor suggestion that it is a crucial feature of the invention that the biotin be substantially free of particulate

**Serial No. 10/762,895**

**Art Unit: 1655**

matter and bacteria. In addition, Shirai et al. is completely silent concerning the production of polycarboxylic acids by the process. In addition, Shirai et al. teaches that the source of vitamins, amino acids and other gross factors can be for example corn steep liquor, peptones, yeast extract, etc. Applicants respectfully submit that this is not biotin substantially free of particulate matter and bacteria. Applicants therefore respectfully submit that Shirai et al. is deficient in neither teaching nor suggesting the present invention.

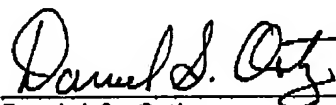
The deficiencies in Shirai et al. are not cured by Mobley et al. Mobley et al. discloses a fermentation medium which can contain components such as corn steep liquor and the like. Applicants submit that use of corn steep liquor would teach one skilled in the art away from the present invention. In addition, Mobley et al. teaches that the transformation is carried out at a pH in the range above pH 7 and preferably in the range of 7.8. Applicants therefore respectfully submit that Mobley et al. would teach one skilled in the art away from the present invention.

The deficiencies in the combination of Shirai et al. and Mobley et al. are not cured by combination with Takahashi et al. As pointed out above, Takahashi et al. is directed to a process which utilizes corn steep liquor and other materials such as meat extract, peptones and casein hydrolysate. Applicants therefore respectfully submit that Takahashi et al. does not cure the deficiency in the combination of Shirai et al. with Mobley et al.

**Serial No. 10/762,895**  
**Art Unit: 1655**

In view of the amendments entered in the claims and above discussion, Applicants respectfully submit that the application is in condition for allowance and favorable consideration is requested.

Respectfully submitted,



Daniel S. Ortiz  
(Reg. No. 25,123)  
Attorney for Applicants  
(215) 628-1141

Cognis Corporation, Patent Dept.  
300 Brookside Avenue  
Ambler, PA 19002

DSO/ras

H:\AMEND\16560B.AMD.DOC